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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/595,195	06/16/2000	Sanjay Nigam	SD9-141-2	1117

41790 7590 05/31/2005

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EXAMINER	
FORD, ALLISON M	
ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 05/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/595,195	NIGAM ET AL.	
	Examiner	Art Unit	
	Allison M. Ford	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *2-4,8,9 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-7,10 and 12* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 June 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments/Amendments

Applicant's arguments filed 14 March 2005 have been fully considered but they are not persuasive. Applicant's amendments to claims 1, 5, 7, 10 and 12 have been entered. Claims 1-12 are pending in the current application, with claims 2-4, 6, 8-9 and 11 being withdrawn from consideration.

Claim Objections

Applicant has adopted the lettering/numbering system suggested by the examiner for clarity in claim 1; however, the following informality was noted: the letter "d" was omitted from the step comprising "culturing the combined tissue under conditions to ensure continued vasculogenesis to obtain a vascularized mammalian tissue..." It would be remedial to add "d" into the letter/number scheme.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5-7, 10 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for constructing a mammalian tissue or a fragment thereof, comprising the method of claim 1, wherein the conditioned medium is BSN cell cultured medium (BSN-CM), does not reasonably provide enablement for construction of a mammalian tissue or a fragment thereof, comprising the method of claim 1, wherein the conditioned medium is 3T3 fibroblast cell conditioned medium, immortalized UB cell conditioned medium, or mIMCD cell conditioned medium. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicant's invention clearly requires the use of BSN cell cultured medium, as applicant's have specifically pointed out that use of other conditioned mediums, such as 3T3 fibroblast cell conditioned medium, immortalized UB cell conditioned medium or mIMCD cell conditioned mediums are not capable of promoting extensive branching morphogenesis of isolated ureteric buds (See Spec. Pg. 13). While applicant's teach BSN-CM to be the conditioned medium used in the method, they do not unequivocally define the term "conditioned medium" to refer solely to BSN-CM; therefore, as written claim 1 refers to use of any conditioned medium. It would be remedial to specifically claim BSN-CM as the conditioned medium in claim 1.

Claim 6 remains rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant describes a method for inducing vasculogenesis of epithelial derived cells in metanephric mesenchymal tissue by the steps enumerated above. Cells are to be cultured in a conditioned medium, which is defined in the specification to be the culture medium obtained by washing a confluent monolayer of BSN cells with serum-free medium, culturing the BSN cells in serum free medium for 2-4 days, and then harvesting and concentrating the medium (See Specification Pg 18-19). Applicant teaches that the BSN culture medium (BSN-CM) has an unidentified growth promoting constituent and/or inducer of differentiation. However, because this factor remains unidentified applicant is relying on the inherent property of the factors found in the medium; they have not provided sufficient written description and characterization of the growth promoting constituent and/or inducer of differentiation present in the BSN-CM to adequately identify these constituents (See Specification Pg 9). Applicant has not provided the necessary disclosure of relevant, identifying characteristics, such as structure or other physical or

chemical properties, or functional characteristics, beyond disclosure of the generic action inherent to the growth medium, sufficient to show the applicant was in possession of the claimed matter. *See Eli Lilly,* 119F. 3d. at 1568, 43 USPQ2d at 1406. See MPEP § 2163.

Applicant traverses that claim 6 is not claiming the constituent, but merely further defining the "conditioned medium" as comprising such a constituent. However, the examiner maintains that while one may claim a *defined* inherent property, one cannot claim an *unidentified* inherent property of a culture medium. Applicant's teach the importance of the BSN-CM, but remain unable to identify the actual constituent (See Spec, Pg. 23-26). Therefore it remains that applicant has not provided the necessary disclosure of relevant, identifying characteristics, such as structure or other physical or chemical properties, or functional characteristics, beyond disclosure of the generic action inherent to the growth medium, sufficient to show the applicant was in possession of the claimed matter. While applicants may have been in possession of the conditioned medium, they are not in possession of the unidentified critical factor, because they are unable to elucidate what it is.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5-7, 10, and 12 are rejected under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's claim 1 requires the use of "conditioned medium." It appears applicant is intending to require the use of BSN cell conditioned medium (BSN-CM); however, the term "conditioned medium" is not specifically defined in the specification to solely refer to BSN-CM. In example 2 applicants teach the conditioned medium used for the culture of the ureteric bud branch tips and metanephric

mesenchymal tissue to be BSN-CM; but use of the BSN-CM in the examples is not sufficient to unequivocally define the term "conditioned medium" to be BSN-CM in the claims, especially when other conditioned mediums are mentioned in the specification (See Pg. 13, Fig 5: 3T3 fibroblast conditioned medium, immortalized UB cell conditioned medium, mIMCD cell conditioned medium). It would be remedial to specifically claim BSN conditioned medium as the conditioned medium in the method of claim 1.

Applicant's claim 1(a)(ii) reads, "permitting the tissue or cells to form multiple branches;" it is unclear what is meant by the tissue or cells forming branches. Most cells or tissues will grow to a confluent monolayer, it is not clear if these cultures are to form dendrite-like projections, or what induces them to form what applicant calls 'branches.'

Applicant's claim 1 (a)(iv) and 1 (b)(ii) have been amended to claim the respective culturings are done in the presence of medium, serum, at least one growth factor, and conditioned medium. It is not clear how "medium" is different than "conditioned medium."

Applicant's claim 1(b)(iv) remains rejected because it was not clear that the fetal metanephric mesenchyme was initially cultured on a substrate, so it is not clear how vasculogenesis is induced by substrate deprivation. And it remains unclear what constitutes the soluble factors which are added to induce vasculogenesis.

Applicant's claim 1(c) requires combining each vascularized mesenchyme with each cultured branch tip bud in a matrix. It remains unclear how the bud and mesenchyme are combined, if they are placed next to one another, if they are infused in some way, if a physical connection is made, etc, this combining is not clear. The specification only teaches the Ureteric Buds were "recombined with freshly isolated E-13 rat metanephric mesenchyme" (See Specification Pg 20), it does not provide any information on how the (re)combination occurs.

Finally, applicant's claim 1(d) remains rejected as being unclear on what comprises the conditions that ensure continued vasculogenesis. The specification teach the combined Ureteric buds and metanephric mesenchyme are cocultured on a transfilter for 5 days in DMEM/F12, plus 10% FCS (See Specification, Pg 20); it is not clear if these are the conditions required for vasculogenesis, or if other actions are needed.

Applicant's claim 6 requires the conditioned medium to comprise a growth promoting constituent or inducer of differentiation or morphogenesis. The specification teaches a conditioned medium of concentrated culture medium obtained by washing a confluent monolayer of BSN cells with serum-free medium, culturing the BSN cells in serum free medium for 2-4 days, and then harvesting and concentrating the medium (See Specification Pg 18-19). This definition does not provide evidence of a growth promoting constituent or inducer of differentiation; therefore it is not clear what these growth promoting constituents or inducers of differentiation consist of.

It remains that applicant is unable to particularly point out and claim the invention, as they are unable to distinctly claim the unidentified factor found in the conditioned medium. While applicants may have been in possession of the conditioned medium, they are not in possession of the unidentified critical factor, because they are unable to elucidate what it is.

Double Patenting

Claims 1 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26, 29, and 38 of copending Application No. 10/608,783. The method of claims 26, 29 and 38 of copending application 10/608,783 are directed to a method of culturing uteric bud cells and metanephric mesenchyme cells in a BSN cell conditioned medium, and then allowing the cells to interact to stimulate branching tubular morphogenesis. Although the conflicting claims are not identical, they are not patentably distinct from each other because both

methods require culture of uteric bud cells and metanephric mesenchyme in BSN cell conditioned medium and then subsequent interaction of the two cell types to form a vascularized mammalian kidney tissue. Though the copending claims do not require the particular culturing steps of the uteric bud cells or metanephric mesenchyme that are claimed in steps (a) and (b) of the current application, the culturing steps (a) and (b) appear to be obvious culture steps for propagation of the cell types, and would be obvious to one of ordinary skill in the art; therefore both methods effectively claim the same method of forming the vascularized mammalian kidney tissue.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Allison M Ford whose telephone number is 571-272-2936. The examiner can normally be reached on M-F 7:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Allison M Ford
Examiner
Art Unit 1651

LEON B. LANKFORD, JR.
PRIMARY EXAMINER